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Formulation and Evaluation of Diclofenac Diethylamine Gel Using Natural Mucilages

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ABSTRACT
Gels have better potential as a vehicle to deliver the drug topically. The present work aimed to study the gelling efficiency of natural mucilages using diclofenac diethylamine used topically for its effective anti-inflammatory and analgesic properties. Diclofenac diethyl amine topical gels were formulated with okra mucilage (2.5-10%), and hibiscus mucilage (2.5-10%) and compared with Carbopol 934 (1-2%). The prepared gel formulations were evaluated for clarity, homogeneity, pH, spreadability, extrudability, and drug content. Formulation F4 containing 10% Hibiscus mucilage as the gelling agent was chosen as the optimized formulation after all the physicochemical tests. Okra mucilage and hibiscus mucilage were proven as efficient gelling agents in the preparation of diclofenac diethyl amine topical gels**.**

Key words: Okra mucilage, Hibiscus mucilage, Diclofenac diethyl amine, gels**.**

I. INTRODUCTION:

Natural Mucilages

Natural mucilages comprise a large macromolecular structure of repeating units(polymers).According to the chemical structural orientation of mucilage, subunits are connected by covalent bonding, irrespective of natural or synthetic mucilage. The availability of natural mucilage and its utilization in pharmaceutical preparation is widespread due to its availability, biodegradability, economic, and non-toxicity[1]. These mucilages, which are original in a natural way, have many potential-oriented tasks. For example, the quantity of compound isolated is minimal and has a complex structure in mixtures. This is due to the different habitations of the plants and seasonal conditions. That affects the isolation and purification methods of the natural mucilages, which are slow and high-cost value[2].

Utilization of the natural mucilages (polymer) in pharmaceutical preparation such as gelling films, microsphere beads, solid monolithic matrix systems, nanoparticles, implants, tablets, injection, emulsion, suspension, and Cosmetic products. In these pharmaceutical formulations, the natural polymer is used as a binding, coating, suspending, emulsifying, gelling, and sustained-release agent[3]. Gums and mucilages contain hydrophilic molecules that can combine with water to form viscous or gel-like solutions[4].Natural Mucilages used in Topical Gel Formulations include okra,hibiscus, aloe Vera, guar gum,xanthan gum, and fenugreek[5].

These mucilages can be incorporated into various topical formulations such as moisturizers, anti-inflammatory gels, and wound healing gels[6].

Gels

Gels are transparent or translucent semisolid formulations containing a high ratio of solvent and gelling agent. When dispersed in an appropriate solvent, gelling agents merge or entangle to form a three-dimensional colloidal network structure, which limits fluid by entrapment and immobilization of the solvent molecules[7]. Typical polymers used as gelling agents include natural, gums, synthetic, and semisynthetic polymers[8].

II. MATERIALS AND METHOD

Dr Reddy's Laboratories, Hyderabad, India, kindly donated Diclofenac diethylamine as a gift sample. Hibiscus, okra (collected from the local market), Carbopol 934, propylparaben, methylparaben, and triethylamine were procured from SD fine Chemicals Maharashtra, India Propylene glycol was purchased from Sigma Aldrich.

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DICLOFENAC DIETHYLAMINE

Diclofenac diethylamine is a well-established NSAID agent used for a variety of painful and inflammatory conditions. It is available in topical dosage forms like gel,lotion,creams, ointment, and as aparenteral dosage form[9]. A topical diclofenac product with a higher concentration of the active ingredient does not necessarily lead to greater absorption relative to a product with a lower concentration of the active ingredient but different characteristics[10].

Hibiscus

Hibiscus rosa sinensis Linn. (Malvaceae) is a glorious shrub widely cultivated in the tropics. It is well-accepted that the leaves and flowers of Hibiscus rosa-sinensis have hair growth-promoting and anti-greying properties. Moreover, in India, the herbal products in the market intended for hair growth include the extract of various parts of Hibiscus rosasinensis Linn. The flavonoids like Quercetin and Rutin present in the Hibiscus leaf extract are responsible for the anti-inflammatory activity. Hibiscus mucilage is also widely used as an adjuvant in pharmaceutical preparations[11].

Active Constituents of Hibiscus: anthocyanins and polyphenols, flavonoids, terpenoids, tannins, cardiac glycosides[12]

Okra

Okra (Abelmoschus esculentus) is the only vegetable crop of significance in the Malvaceae family. It provides the highest bio-adhesive strength. Okra is an effective remedy for ulcers and joint healthiness. It is used to counteract the acids due to its alkaline origin. It also guards the mucous membranes of the digestive system. Okra contains special fibersthattake sugar levels in the blood under control[13].

Active constituents of Okra: vitamin C, carotene,thiamine, folic acid, riboflavin, oxalic acid, niacin, and amino acids[14].

Okra gum contains polysaccharides comprising rhamnose, galactose, glucose, galacturonic acid, and glucuronic acid. The properties of okra gum are then elaborated and is also used as a binder in gel formulations[15].

Methodology

Isolation of Hibiscus Mucilage

The fresh leaves of Hibiscus rosa-sinensis were collected, washed with water to remove dirt and debris, and dried for a few days.The dried leaves were blended to a fine powder, transferred to a beaker containing water, soaked for 12 - 24 h, and filtered through muslin cloth to collect the extract.The above extract was treated with acetone with continuous stirring to isolate the mucilage.The mucilage was separated and dried in a hot air oven at 100℃ for 3-4 hr to get fine powder[16].

Isolation of okra Mucilage

Properly cleaned and sliced okra (1 kg) was dried for 5 days.Further, it is dried in a hot air oven at 40^{o} C for 5 - 6 h to obtain constant weight.Dried okra was blended into fine powder. The okra powder was transferred to a beaker containing water, soaked for 12 - 24h, and filtered through muslin cloth to collect the extract.The above extract was treated with acetone with continuous stirring to isolate mucilage.The collected mucilage was dried at a temperature of 100°C in a hot air oven for 3 hours to get fine powder[17].

Formulation of diclofenac diethylamine gels Preparation of diclofenac diethylamine gels using natural mucilages. The gels were formulated by adding different concentrations (2.5%, 5%, 7.5%, 10%) of okra gum powder as a gelling agent in lukewarm distilled water with constant stirring by using a magnetic stirrer. Then accurately weighed quantity of diclofenac diethylamine was dispersed in methanol and poured into the above natural gum base, propylene glycol, and methylparaben were added as humectant and preservative respectively. pH of the gels was adjusted using triethanolamine. The procedure was repeated using hibiscus gum powder to prepare other sets of gels.

Preparation of diclofenac diethylamine gels using synthetic polymer

Other sets of gels were formulated using the synthetic polymer Carbopol 934 as a gelling agent. The gels were formulated by dispersing different concentrations (1%, 1.5%, 2%) of Carbopol 934 in distilled water with constant stirring using a magnetic stirrer. An accurately weighed quantity of the drug was dispersed in methanol and poured into the above synthetic gel base, propylene glycol, and methylparaben were added as humectant and preservative respectively. pH of the gels was adjusted using triethanolamine.

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Table no.1 Formulation of diclofenac diethyl amine gels

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
Diclofenac diethyl amine (%)	1.16	1.16	1.16	1.16	1.16	1.16	1.16	1.16	1.16	1.16	1.16
Hibiscus mucilage (%)	2.5	5	7.5	10	-	-	-	-	-	-	-
Okra mucilage (%)	-	-	-	-	2.5	5	7.5	10	-	-	-
Carbopol 394	-	-	-	-	-	-	-	-	1	1.5	2
Propylene glycol(ml)	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Methylparaben (%)	0.045	0.045	0.045	0.045	0.045	0.045	0.045	0.045	0.045	0.045	0.045
Methanol (ml)	2	2	2	2	2	2	2	2	2	2	2
Distilled water(ml)	QS	QS	QS	QS	QS	QS	QS	QS	QS	QS	QS

Evaluation of diclofenac diethyl amine gels

The prepared gels of diclofenac dimethylamine were evaluated for color, homogeneity, pH determination, Spreadability, and drug content.

- **Color**
  The formulations were viewed for their visual appearance.

- **Homogeneity**
  All developed gels were tested for the absence of particles, aggregates, and fibers by visual inspection.

- **Extrudability**

The formulation is filled in the collapsible tubes after the gels are set in the container. Extrudability is based upon the quantity of gel in percentage and gel extruded from a collapsible tube on the application of weight in grams required to extrude at least 0.5 cm ribbon of gel in 10 seconds.

- **Drug content**

In an appropriate solvent, 1 gm of gel was mixed and filtered to obtain a clear solution. The absorbance was determined by a UV spectrophotometer, and the absorbance values were used to determine the drug content.

- **Spreadability**

The spreadability of the prepared formulations was determined by measuring the spreading diameter of 1g of the gel between 20×20cm glass plates after 1 min. The mass of the upper plate was standardized at 50g. The spreadability was calculated using the formula

$S=\pi r^2/w$

Where,
S=Spreadability
R=radius
W=weight placed on the plate

Determination of pH of the prepared gels

pH was checked using pH meter (Systronics digital pH meter). The electrode was submersed into the formulations at room temperature and readings were noted.

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III. RESULTS AND DISCUSSIONS

Evaluation of diclofenac diethyl amine gels

The formulated gels were evaluated for all the physicochemical parameters and reported in Table 2

Table no.2physicochemical characteristics of gels

Gel	Color	odor
Carbopol	Transparent	-
Hibiscus mucilage	Dark green	Sweet, floral
Okra mucilage	Light green	Mild, almost grassy flavor

From the above table, the color of Carbopol was found to be transparent in color, whereas hibiscus and okra mucilage gels are dark green and light green respectively.

Homogeneity

It was evaluated by visual observation. All the formulations were found to be homogenous and clear. Indicates good homogeneity of the formulations.

Extrudability

Extrudability was performed and all the gel formulations showed smooth flow properties.

pH

pHof all the formulations were evaluated using a pH meter and reported in Table 4

Table no.4 pH of the prepared gels

Formulation	pH
F1	7.5
F2	6.8
F3	7.3
F4	6.7
F5	7.2
F6	6.69
F7	7.4
F8	7.8
F9	8.0
F10	7.8
F11	7.84

The P^H was found in the range of 6.75 to 8.0. This slightly acidic to slightly basic range helps ensure the stability and efficacy of the medication

Spreadability: All the gel formulations were evaluated for spreading efficiency and the results were reported in Table 3.

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Table no. 3 Spreadability of F1-F11 formulations

Gels	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
Carbopol	4.2cm	4.6cm	4.4cm	4.8cm	-	-	-	-	-	-	-
Hibiscus mucilage	-	-	-	-	4.7cm	4.5cm	4.6cm	-	-	-	-
Okra mucilage	-	-	-	-	-	-	-	-	4.5cm	4.3cm	4.1cm

The Spreadability of gels was found to be in the range of 4.1 cm to 4.8 cm. It has fairly good Spreadability. It is easily applied without too much rubbing. So, the diffusion of the drug into the skin can be increased.

IV. CONCLUSION

The property of hibiscus and okra mucilages as gelling agents in the topical gel formulations was studied. For the study, the concentration of mucilages ranging from 2.5-10% was used to prepare gel formulations and were compared with synthetic gelling agent Carbopol 934 from 1-2%. In this diclofenac diethylamine was used as a model drug having anti-inflammatory and analgesic activities. Different evaluation tests were performed and results were compared with a gel formulated using a synthetic gelling agent. F4 formulation containing 10% hibiscus mucilage as a gelling agent is chosen as the optimized formulation. From the above study, it can be concluded that the topical gel prepared from the natural mucilages is superior to the gels prepared with synthetic gelling agents but should be used in higher concentration than the synthetic gelling agents, which supports several studies on natural gelling agents suggesting them to be advantageous, economic and less toxic as compared to synthetic ones.

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